REMARKS

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

I. Restriction requirement and unity of invention

Claims directed to methods of using the polynucleotides for detecting polynucleotides by hybridization and/or PCR (i.e., Claims 34-36), for assessing toxicity of a test compound (i.e., Claim 44), and for screening for effectiveness in altering expression (i.e., Claim 43), could and should be examined together with the product claims from which they depend, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Applicants presume that these method claims will be rejoined, upon determining allowability of the product claims from which they depend.

In addition, Applicants request withdrawal of the holding of lack of unity of invention between claims drawn to polynucleotides and claims drawn to the polypeptides encoded by the polynucleotides (i.e. Claims 21-23 and 37-42).

The Patent Office asserts that "[t]he polynucleotide of claim 33, which is drawn to an isolated polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:31, encompasses polynucleotides that, when expressed, results in the production of proteins that do not correspond to the polypeptide of SEQ ID NO:2. Therefore, the polynucleotide of Group XXXI, particularly the polynucleotide of claim 33, does not share a corresponding special technical feature with the polypeptide of Group II, and thus the inventions do not have unity of invention". (Office Action, October 17, 2003; page 3). The Office further asserts that "the technical feature of Group XXXI is a polynucleotide, which is shown by Database GenBank Accession Number AC004241 (GI 3108007) to lack novelty or inventive step because Database GenBank Accession Number AC004241 teaches a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:31." (Office Action, October 17, 2003, pages 3-4).

To expedite prosecution of the subject application, the "fragment" language has been deleted from Claims 21 and 32; and Claim 33 has been cancelled. Applicants expressly do not

disclaim equivalents of the claimed subject matter.

Applicants respectfully submit that in light of the claims currently amended in this paper, unity of invention clearly does exist between claims drawn to polynucleotides (i.e. Claims 30, 32, 34-36, and 43-44) and claims drawn to the polypeptides encoded by the polynucleotides (i.e. Claims 21-23 and 37-42).

II. Claim Objections

Claims 27-30 have been amended as suggested by the Examiner (Office Action, October 17, 2003, pages 6-7). Claims 33 and 45 have been cancelled. As discussed above, unity of invention exists between the "polynucleotide " and "polypeptide" claims. Accordingly, Claims 24-26 have not been placed in independent form. Withdrawal of the objection to the cliams is therefore requested.

III. Indefinitness rejections under 35 U.S.C. § 112, second paragraph

Claim 21 has been amended by deleting the recitation of a "biologically active fragment". Claim 32 has been amended to recite a polynucleotide that is "fully complementary". By these amendments, Applicants expressly do not disclaim equivalents of the invention which could include polynucleotides encoding biologically active fragments of SEQ ID NO:2. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the instant application. Therefore, withdrawal of this rejections is requested.

IV. Utility rejection under 35 U.S.C. § 101 and § 112, first paragraph

Claims 24-30, 32-33, and 45 stand rejected under 35 U.S.C. § 101 and § 112, first paragraph based on the allegation that the claimed invention lacks patentable utility. The rejection alleges in particular that:

- "...the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility". (Office Action, October 17, 2003; page 8).
- "...since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention". (Office Action,

October 17, 2003, page 9).

The rejection of Claims 24-30, 32-33, and 45 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well known to one of ordinary skill in the art.

The invention at issue is a polynucleotide corresponding to a cAMP-regulated guanine nucleotide exchange factor that is expressed in reproductive, nervous, and cardiovascular tissues in humans. The claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptide coded for by the polynucleotide actually functions.

Applicants submit with this paper two expert Declarations under 37 C.F.R. § 1.132, with respective attachments, and ten (10) scientific references filed before or shortly after the November 23, 1998 priority date of the instant application. The Rockett Declaration and the Iyer Declaration, and the ten (10) references establish that, prior to the filing dates of the provisional applications to which the subject application is benefitted priority, it was well-established in the art that:

> polynucleotides derived from nucleic acids expressed in one or more tissues and/or cell types can be used as hybridization probes -- that is, as tools -- to survey for and to measure the presence, the absence, and the amount of expression of their cognate gene;
>
> with sufficient length, at sufficient hybridization stringency, and with sufficient wash stringency -- conditions that can be routinely established -- expressed polynucleotides, used as probes, generate a signal that is specific to the cognate gene, that is, produce a gene-specific expression signal;
>
> expression analysis is useful, *inter alia*, in drug discovery and lead optimization efforts, in toxicology, particularly toxicology studies conducted early in drug development efforts, and in phenotypic characterization and categorization of cell types, including neoplastic cell types;
>
> each additional gene-specific probe used as a tool in expression analysis provides an additional gene-specific signal that could not otherwise have been detected, giving a more comprehensive, robust, higher resolution, statistically more significant, and thus more useful expression pattern in such analyses than would otherwise have been possible;
>
> biologists, such as toxicologists, recognize the increased utility

of more comprehensive, robust, higher resolution, statistically more significant results, and thus want each newly identified expressed gene to be included in such an analysis;

nucleic acid microarrays increase the parallelism of expression measurements, providing expression data analogous to that provided by older, lower throughput techniques, but at substantially increased throughput;

accordingly, when expression profiling is performed using microarrays, each additional gene-specific probe that is included as a signaling component on this analytical device increases the detection range, and thus versatility, of this research tool;

biologists, such as toxicologists, recognize the increased utility of such improved tools, and thus want a gene-specific probe to each newly identified expressed gene to be included in such an analytical device;

the industrial suppliers of microarrays recognize the increased utility of such improved tools to their customers, and thus strive to improve salability of their microarrays by adding each newly identified expressed gene to the microarrays they sell;

it is not necessary that the biological function of a gene be known for measurement of its expression to be useful in drug discovery and lead optimization analyses, toxicology, or molecular phenotyping experiments;

failure of a probe to detect changes in expression of its cognate gene does not diminish the usefulness of the probe as a research tool; and

failure of a probe completely to detect its cognate transcript in any single expression analysis experiment does not deprive the probe of usefulness to the community of users who would use it as a research tool.

The Patent Examiner does not dispute that the claimed polynucleotide can be used as a probe in cDNA microarrays and used in gene expression monitoring applications. Instead, the Patent Examiner contends that the claimed polynucleotide cannot be useful without precise knowledge of its biological function, or the biological function of the polypeptide it encodes. But the law has never required knowledge of biological function to prove utility. It is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the utility requirement.

In any event, as demonstrated by the Rockett Declaration and the Iyer Declaration the person of ordinary skill in the art can achieve beneficial results from the claimed polynucleotide in the absence of any knowledge as to the precise function of the protein encoded by it. The uses

of the claimed polynucleotide in gene expression monitoring applications are in fact independent of its precise biological function.

V. Written description rejections under 35 U.S.C. § 112, first paragraph

Claims 24, 26, 28-30, 32-33, and 45 were rejected under 35 U.S.C. § 112, first paragraph, as being based on a specification which allegedly fails to reasonably convey to one of skill in the art that the Applicants had possession of the claimed invention at the time the application was filed. The Office Action asserts that "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention". (Office Action, October 17, 2003; page 10). This rejection is traversed.

Claim 21 has been amended by deleting the "fragment" language. In addition, the polynucleotide fragments recited by Claim 33 have been cancelled. By these amendments, Applicants expressly do not disclaim equivalents of the invention. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the instant application.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. (citations omitted.)

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

A. The specification provides an adequate written description of the recited "variants" of SEQ ID NO:2

The subject matter encompassed by claims 24, 28-30, and 32 is either disclosed by the Specification or is conventional or well known to one skilled in the art.

First note that the "variant" language of independent Claim 24 recites a polypeptide comprising "a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:2." The amino acid sequence of SEQ ID NO:2 is explicitly disclosed in the Specification, as is the polynucleotide sequence of SEQ ID NO:31. See, for example, the Sequence Listing. Variants of GTPAP are described, for example, at page 5, lines 24-26 and lines 28-32; page 6, lines 12-14; page 19, line 28 to page 20, line16.

One of ordinary skill in the art would recognize naturally occurring amino acid sequences which are variants at least 90% identical to SEQ ID NO:2. Given any naturally occurring amino acid sequence, it would be routine for one of skill in the art recognize whether it was a variant of SEQ ID NO:2. Accordingly, the Specification provides an adequate written description of the recited variants of SEQ ID NO:2.

There simply is no requirement that the claims recite particular amino acid "variant" sequences because, as discussed above, the Specification already provides sufficient structural

definition of the claimed subject matter. Because the recited amino acid "variants" are defined in terms of SEQ ID NO:2, the precise chemical structure of every amino acid variant within the scope of the claims can be discerned. Accordingly, the Specification provides an adequate written description of the claimed sequences. The Examiner's position is nothing more than a misguided attempt to require Appellants to unduly limit the scope of their claimed invention.

1. The present claim specifically defines the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides encoding polypeptides in terms of chemical structure, rather than on functional characteristics. For example, the "variant" language of independent Claim 21 recites chemical structure to define the claimed genus:

Claim 21:

21. An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, and

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:2.

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:2. In the present case, there is no reliance merely on a description of functional characteristics of the polypeptides which are encoded by the polynucleotides. The polypeptide, defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant". Available evidence illustrates that, rather than being a large variable genus, the claimed genus is of narrow scope.

In support of this assertion, the Board's attention is directed to the enclosed reference by Brenner et al. (Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships, Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078; Reference No. 7). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to polynucleotides encoding polypeptides related to the amino acid sequence of SEQ ID NO:2. In accordance with Brenner et al., naturally occurring molecules may exist which could be characterized as GTPase associated proteins and which have as little as 30% identity over at least 150 residues to SEQ ID NO:2. The "variant language"of the present claims recites, for example, polynucleotides encoding a polypeptide

comprising "a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:2." This variation is far less than that of all potential GTPase associated proteins related to SEQ ID NO:2, i.e., those GTPase associated proteins having as little as 30% identity over at least 150 residues to SEQ ID NO:2.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of November 23,1998. Much has happened in the development of recombinant DNA technology in the 17 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:2 and SEQ ID NO:31, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide "variants" at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:2. The courts have stressed that

structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides which encode the polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

For at least the above reasons, withdrawal of this rejection is requested.

VI. Enablement rejections under 35 U.S.C. § 112, first paragraph

The rejection set forth in the Office Action is based on the assertions discussed above, i.e., that the claimed invention lacks patentable utility (Office Action, October 17, 2003, page 11). To the extent that the rejection under § 112, first paragraph, is based on improper allegation of lack of patentable utility under § 101, it fails for the same reasons.

In addition, Claims 24, 26, 28-30, 32-33, and 45 were rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the specification does not describe the subject matter of the invention in such a way as to enable one of skill in the art to make and/or use the claimed variants and fragments. In particular, the Office Action asserts that "the specification, while being enabling for a polynucleotide of SEQ ID NO:2, does not reasonably provide enablement for polynucleotides of any function (1) encoding polypeptides having at least 90% structural identity to SEQ ID NO:2, (2) having at least 90% structural identity to SEQ ID NO:31, or (3) comprising at least 60 contiguous nucleotides of SEQ ID NO:31." (Office Action, October 17, 2003, page 11).

Claim 21 has been amended by deleting the "fragment" language. Claim 33 has been cancelled. By these amendments, Applicants expressly do not disclaim equivalents of the invention. Applicants do not concede to the Patent Office position; Applicants are amending the claim solely to obtain expeditious allowance of the instant application.

With respect to the claimed polynucleotide "variants", the Office Action asserts that "small structural changes can result in a polypeptide having different function, therefore the claimed polynucleotides can potentially encode proteins of many different functions which cannot be inferred by structural homology alone." (Office Action, October 17, 2003; page 13).

Note that Claim 21, for example, recites not only that the polypeptide variants are at least 90% identical to SEQ ID NO:2, but also that they have "**a naturally occurring amino acid sequence**." Through the process of natural selection, nature will have determined the appropriate amino acid sequences. Given the information provided by SEQ ID NO:2 (the amino acid sequence of GTPAP-2) and SEQ ID NO:131 (the polynucleotide sequence encoding GTPAP-2), one of skill in the art would be able to routinely obtain "a naturally occurring amino acid sequence at least 90% identical to" the amino acid sequence of SEQ ID NO:2.

For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the specification of the instant application. See, e.g., page 15, line 16 to page 16, line 9; page 40, lines 16-26; and Example VI at page 50. Thus, one skilled in the art need not make and test vast numbers of polynucleotides that encode polypeptides based on the amino acid sequence of SEQ ID NO:2, or vast numbers of polynucleotides based on the polynucleotide sequence of SEQ ID NO:31. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides, and their encoded polypeptides, that already exist in nature. By adjusting the nature of the probes or nucleic acids (i.e., non-conserved, conserved, or highly conserved) and the conditions of hybridization (maximum, high, intermediate, or low stringency), one can obtain variant polynucleotides of SEQ ID NO:31 which, in turn, will allow one to make the variant polypeptides of SEQ ID NO:2 recited by the present claims using conventional techniques of recombinant protein production. By extension, one of skill in art could make fragments of naturally occurring polynucleotides at least 90% identical to SEQ ID NO:31, and could use such fragments, for example, as hybridization probes to detect full-length naturally occurring polynucleotides at least 90% identical to SEQ ID NO:31. Similarly, a skilled artisan could make polynucleotides encoding fragments of the SEQ ID NO:2 polypeptide, and could use such fragments, for example, as hybridization probes to detect polynucleotides encoding full-length human variants of the SEQ ID NO:2 polypeptide.

Furthermore, the identity of amino acids in GTPAP-2 which are tolerant of modification and/or which are conserved has no bearing on the ability of a skilled artisan to screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides, and their encoded polypeptides, that already exist in nature, without undue experimentation. Moreover, it is irrelevant whether any of the claimed polynucleotides encode polypeptide variants which have any biological functions at all. One of skill in the art would still know how to make and use such

polynucleotides, without undue experimentation. For example, polynucleotides which encode nonfunctional polypeptide variants of SEQ ID NO:2 could be used to detect polynucleotides which encode the polypeptide of SEQ ID NO:2 by, for example, hybridization and/or PCR techniques. It is not necessary for a polynucleotide to encode a functional polypeptide for one of skill in the art to be able to use that polynucleotide without undue experimentation.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Office Action has failed to provide any **reasons** why one would doubt that the guidance provided by the present Specification would enable one to make and use the recited polynucleotides encoding polypeptide variants of SEQ ID NO:2 or the recited polynucleotide variants of SEQ ID NO:31. Hence, a *prima facie* case for non-enablement has not been established with respect to the recited variants of SEQ ID NO:2 and SEQ ID NO:31.

For at least the above reasons, withdrawal of this rejection is requested.

VII. Rejection under 35 U.S.C. § 102(a)

Claims 24-26 and 33 were rejected under 35 U.S.C. § 102(a) because they are allegedly anticipated by Muzny et al. (GenBank accession number AC00241 GI3108007, May 2, 1998). In particular, the Office states that "Muzny et al. teaches a human polynucleotide (158784

nucleotides long) which comprises several fragments of at least 60 nucleotides of the polynucleotide of SEQ ID NO:31. The largest fragment is 1014 nucleotides long." (Office Action, October 17, 2003, page 13).

To expedite prosecution of the subject application, the "fragment" language has been deleted from the claims, including cancellation of Claim 33. Applicants expressly do not disclaim equivalents of the claimed subject matter.

Moreover, Muzny et al. is not pertinant to the claimed "full length" sequences. That is, Muzny et al. appears to describe a genomic DNA which has numerous intervening sequences interspersed between coding segments of DNA. The present claims, however, do define polynucleotides that are "full length" polynucleotides which encode the amino acid sequence of SEQ ID NO:2, or "variants" which are at least 90% identical thereto. Such "full length" polynucleotides do not contain intervening sequences.

Accordingly, Muzny et al. does not anticipate the claims, and withdrawal of this rejection is believed to be in order.

Please charge Deposit Account No. **09-0108** in the amount of **$110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. 09-0108.

Respectfully submitted,

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Limited Recognition (37 C.F.R. 10.9 (b)) attached

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